REMARKS/ARGUMENTS

I. Amendments to the Specification:

Consideration and entry by the Examiner of amendments correcting several minor errors to the specification is appreciated. However, corrections to the specification have been denied on the basis of new matter in paragraphs [0010], [0033 - 0034], [0040], [0064], [0069], [0083] and [0085]. Reconsideration is respectfully requested for the following reasons:

In paragraph [0010], it is obvious that the remainder of the sentence was inadvertently left off in the original specification as the sentence ends without an object or period. Support for the amendment is provided in step 2 of Figure 2, which recites "precipitate removal by centrifugation." It is thus clear that the missing part of the sentence should be, at a minimum, "an additional step of centrifugation to remove the precipitated material." The precipitate may alternatively be removed by other methods, including for example filtration as in paragraph [0065], however it is clear from the written description and figures that where employed after lysis and precipitation, centrifugation is for the purpose of removing the precipitated material. This correction is fully supported by the specification including Figure 2 and does not introduce new matter.

Paragraph [0033] continues a written description of the process depicted in Figure 1A. Referring to Figure 1A, two static mixer elements are provided: static mixer **30**, which is situated in-line prior to the entry of precipitating solution from tank **80** through line **90**, and static mixer **70**, which follows the point of entry of the precipitating solution. The first line of paragraph [0033] recites: "The lysis mixture exiting the static mixer **30** then flows through line **60** to static mixer **70**." As static mixer **70** clearly follows static mixer **30** in the in-line process and clearly follows the introduction of precipitating solution to line **60**, it is only possible that "the intersection between lines **60** and **90** can be adjusted so that the lysis mixture and the precipitation solution enter the static mixer [[**30**]] **70** essentially simultaneously" as per the requested correction. This correction is fully supported by the specification including Figure 1A and does not introduce new matter.

Similarly, paragraph [0034] further continues with a written description of the process depicted in Figure 1A and must properly recite that "After exiting static mixer [[30]] 70, the precipitating solution flows through line 100 to centrifuge 110." This correction as to an obvious error is fully supported by the specification including Figure 1A and does not introduce new matter.

In paragraph [0040], it is obvious that the "The column is packed under low pressure, typically less than about [[7]] 0.7 bar." One of skill in the art would not understand 7 bar to be a low pressure packing condition. Furthermore, in the working example disclosed in paragraph [0071], line 7, it is clear the column is packed at 0.7 bar. This correction as to an obvious error is fully supported by the specification and does not introduce new matter.

In paragraph [0064], it is obvious to one of skill in the art that "SM" in the sentence "This solution was then neutralized and cell debris and chromosomal DNA were precipitated by the addition of 16L ice-cold Solution III (3M potassium, [[SM]] 5M acetate, pH 5.5)" cannot be a concentration of acetate. Furthermore, the specification at paragraph [0033] discloses "A suitable precipitating solution is 3M potassium acetate, adjusted to pH 5.5, with acetic acid (~5M acetate final)." This correction as to an obvious error is fully supported by the specification and does not introduce new matter.

Paragraph [0083] has been further amended herein to recite "absolute [[0.2 m]] 0.2 µm nylon filter (Pall Ultipor N_{66})." On page 24, line 5 of the original specification, an empty space conspicuously appears prior to and modifying "m" in the sentence:

> "The neutralized lysate was filtered in series with a nominal 0.2 µm glass filter (Sartorpure GF) and an absolute 0.2 m nylon filter (Pall Ultipor N_{66}) (5 ft^2 each) to reduce bacterial load and endotoxin levels."

If filters exist having a pore size of .2 m (meters), or approximately 8 inches, they would certainly not be expected to reduce bacterial load. Furthermore, the specification at paragraphs [0058] and [0073] clearly teaches discloses filtration through a Pall Ultipor N_{66} 0.2µm nylon

filter. This correction as to an obvious error is fully supported by the specification and does not introduce new matter.

Paragraph [0085] has been further amended herein to recite:

> [0085] The pooled product contained 1787 mg DNA, endotoxin level of 16 EU/mg, and 1.6% genomic DNA. The product was filtered again through [[0.2 m]] 0.2 µm nominal glass and [[0.2 m]] 0.2 µm absolute nylon filters described above. After filtering the product contained endotoxin level of 1 EU/mg and 0.18% genomic DNA, with 94% yield. The filtered product was diafiltered and subjected to a final [[0.2 m]] 0.2 µm sterilization filter as described in Example 1.

Similar to the above amendment to paragraph [0083], in paragraph [0085] it is clear that on page 24, lines 17, 18, and 20 of the originally filed specification that an empty space conspicuously appears prior to and modifying "m" three places. If filters exist having a pore size of .2 m (meters), or approximately 8 inches, they would certainly not be expected to reduce bacterial load. Furthermore, the specification at paragraphs [0058] and [0073] clearly teaches discloses filtration through 0.2µm glass and nylon filters. This correction as to an obvious error is fully supported by the specification and does not introduce new matter.

II. Status of the Claims and Amendments:

Claim 27 has been cancelled and claim 28 has been amended.

III. Double Patenting

Applicant disagrees with the Examiner's determination that prior claims 23 – 43 are obvious in view of a combination of US 6,011,148 and Nochumson, or US 6,011,148, Nochumson and Wan, particularly where it appears that portions of the 6,011,148 specification were impermissibly used in the determination of nonstatutory double patenting. However, in order to advance the issuance of the pending claims, Applicant is submitting a terminal disclaimer herewith. Applicant wishes to make the Examiner aware that the pending Nochumson application is also assigned to the same entity, although at the time the respective applications were filed, the applications were not co-owned.

IV. Rejections under 35 U.S.C. § 102(e)

Claims 23 – 26 and 29 were rejected under 102(e) as anticipated by Nochumson. Claim 23 has been amended to include the limitation of cancelled claim 27, which additionally claimed a step of filtration through a series of filters including one or more glass fiber and nylon filters. Claim 28 has been amended to depend from claim 23 instead of cancelled claim 27. It is respectfully suggested that in light of the present terminal disclaimer and amendments to claim 23 and 28, that no further objections remain to the patentability of 23 – 26, 28 – 36 and 42 – 43. Early acceptance of these claims is respectfully requested.

V. Rejections under 35 U.S.C. § 103

Reconsideration of the Examiner's rejection of claim 37, and dependent claims 38 – 41 on the basis of § 103(a) over the combination of Nochumson, Wan, Lee and Song is respectfully requested. Claim 37, and thus the claims dependant therefrom, are all directed to pharmaceutical scale methods of plasmid DNA purification utilizing several steps including alkaline lysis and precipitation through static mixers, filtration over a series of filters including at least one glass filter and at least one nylon filter, and anion exchange chromatography using a TMAE resin. None of the cited references, alone or in combination, teach or suggest the use of filtration through at least one glass filter and at least one nylon filter in plasmid purification, much less the further combination with alkaline lysis through static mixers and TMAE anion exchange chromatography. Applicants surprising found that this filtration step resulted in significant purification, particularly through the removal of endotoxins, and that this step as well as the combined method is of particular importance in the purification of plasmid DNA at pharmaceutical scale.

Conclusion

For the reasons stated herein, the Applicant respectfully submits that independent claims 23, 33, 37 and 43 are allowable and that the dependent claims are, in turn, also allowable. Applicant respectfully requests allowance of the claims at an early date. The Commissioner is authorized to charge any additional fees incurred in this application or credit

any overpayment to Deposit Account No. 50-1922. Should the Examiner have any questions, please do not hesitate to call Applicant's attorney at 832-446-2421.

Respectfully submitted,

By _____

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